DETAILED ACTION

Status of Claims

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/18/2010 has been entered.

2. Applicant's response, filed 2/18/2010, to the Office Action mailed 8/18/2009 is acknowledged. Applicant has added Claims 3-6 and presented arguments in response to the Office Action.

3. Claims 1-6 are pending and presently under consideration.

4. Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Objections

5. Claims 3-6 are objected to because of the following informalities:

In Claims 3-6, the word "tumor" should more properly be changed to "tumors".

Appropriate corrections are required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for suppressing or inhibiting lung tumorigenesis, does not reasonably provide enablement for preventing the development or recurrence (i.e., curing) of lung tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

To be enabling, the Specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. *PPG v. Guardian*, 75 F.3d 1558, 1564 (Fed. Cir. 1996). (As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation")

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC

1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (Bd. Apls. 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833,839, 166 USPQ 18, 24 (1970). Keeping that in mind, the *Wands* factors are relevant to the instant fact situation for the following reasons:

The nature of the invention, breadth of the claims, state and predictability of the art, and relative skill of those in the art

The instant Specification (at page 5, 1st full paragraph) discloses the instant compound as "an agent effective for preventing lung tumor by suppressing or preventing lung tumorigenesis, a so-called chemopreventive agent for lung tumor." Thus, the Specification is defining "suppressing" lung tumorigenesis to include prevention. Therefore, the claims relate to a method of preventing the development of

lung tumors or preventing the recurrence of lung tumors (i.e., curing lung tumors), comprising administering an effective amount of the compound of Claim 1. The breadth of the claims encompasses the prevention or curing of lung tumors with the compound of Claim 1.

The relative skill of those in the art is high, generally that of an M.D. or Ph.D. The artisan using Applicants' invention would generally be an oncologist with a M.D. degree and several years of experience.

That factor is outweighed, however, by the unpredictable nature of the art. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved" and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ 2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). As long as the Specification discloses at least one method of making and using the claimed invention

that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112, 1st Paragraph is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). To that extent, if little is known in the prior art about the nature of the invention and the art is unpredictable, the Specification would need more detail as to how to make and use the invention in order to be enabling. See *Chiron Corp v. Genetech, Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a specific and useful teaching. The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology."

One skilled in the art would not accept the proposition that lung cancer can be prevented or cured. For example, the Mayo Clinic staff ("Lung cancer: Prevention", 11/2009, MayoClinic.com, downloaded on 3/24/2010, pages 1-3 of 3) teaches lung cancer cannot be prevented although the risk of developing lung cancer can be reduced. See 1st paragraph, at page 1.

The amount of direction or guidance provided and the presence or absence of working examples

The Specification provides an example of the suppression/inhibition of lung tumorigenesis in rats treated with the compound of instant Claim 1. The results are provided in Specification Tables 1 and 2. There is no guidance or working examples for the prevention or cure of lung tumors

The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed compound could be predictably used to prevent or cure lung tumors.

Accordingly, the instant claims do not comply with the enablement requirement of 35 U.S.C. 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tanaka et al. (Cancer Letters, Vol. 172, pages 119-126; previously cited; a copy of the reference is attached), in view of Fan et al., editors ("Mouse Skin tumor Assay", 1996, Toxicology and Risk Assessment: Principles, Methods, and Applications, pages 124-127; previously cited).

Tanaka et al. teach the instantly claimed compound and its high anti-tumor promoting activity. See Abstract and compound 1 on page 121. Tanaka et al. teach

compound 1 "is considered to be a naturally occurring triterpenoind with the strongest anti-tumor promoting activity in the in vivo assay ever known". See page 124, last paragraph. The *in vivo* assay used by Tanaka et al. is a two-stage mouse skin carcinogenesis assay, as described on page 122. The reference discloses that compound 1 is a "promising candidate for effective and safe chemopreventive agents".

Tanaka et al. do not teach the use of the instantly claimed compound (i.e., Tanaka's compound 1) for the treatment of lung tumorigenesis or its oral administration.

Fan et al. teach mouse skin tumor assays and their use as a screening tool for carcinogens and carcinogen promoters. Fan et al. teach a correlation between the mouse skin tumor assay and the mouse lung adenoma assay. Additionally, the reference teaches the use of the skin tumor assays for pharmacological research on chemotherapeutic agents. See pages 124-127, especially the 3rd and 4th paragraphs on page 127. In particular, Fan et al. teach "[t]here also appears to be some correlation between the mouse skin tumor assay and the mouse lung adenoma assay. That is, the lowest dose administered systemically that elicits a positive carcinogenic response appears to be similar with both assays..."

It would have been obvious to one of ordinary skill in the art at the time of the invention combine the teachings of Tanaka et al. and Fan et al. The strong anti-tumor promoting activity of the instantly claimed compound, as taught by Tanaka et al., would have motivated the skilled artisan to test the effectiveness of the compound in inhibiting tumorigenesis in other tissues, including the lung. The teaching by Fan et al. of a correlation between the mouse skin tumor and lung adenoma assays would have

further motivated the artisan to test the compound for effectiveness in inhibiting lung tumorigenesis.

Oral bioavailability of the instantly claimed compound is a characteristic of the compound. If the compound was bioavailable after oral administration, one of ordinary skill in the art would have been motivated to administer the compound by this route for patient convenience and administration compliance.

With regard to Claim 3, it would have been obvious to one of ordinary skill in the art to use the method of treating lung tumorigenesis suggested by Tanaka et al., in view of Fan et al., in treating: a subject who has lung cancer (i.e., "a personal medical history of lung tumor[s]"); or a cigarette smoker, a person exposed to second-hand smoke, or a person working with asbestos (i.e., "environmental factors known [to have a] causal correlation with lung tumorigenesis").

With regard to instant Claims 4-6, administration of the instant compound in a method of treatment for suppressing or inhibiting lung tumorigenesis, as suggested by the prior art presented above, would naturally suppress or inhibit malignant and benign tumors, and prevent the development or recurrence of lung tumors, since the compound of interest taught in the prior art is identical to the instant compound and can not have mutually exclusive properties. See *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Additionally, it is noted that *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product instantly claimed. In such a situation the

burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention"). Also see *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

The instant claims would have been obvious because a person of ordinary skill would have been motivated to combine the prior art (*supra*) to achieve the claimed invention (i.e., treatment of lung tumorigenesis) and that there would have been a reasonable expectation of success.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re*

Opprecht 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

10. Applicant assert Fan et al. teach chemical carcinogenesis in skin is a multistage process and that both Fan et al. and Tanaka et al. teach two-stage mouse skin tumor assays. Applicants allege "that a skilled artisan would not apply the compound of Tanaka to suppress or inhibit *lung* tumorigenesis because such tumorigenesis is not known to be a multistage process as taught by Tanaka and Fan."

Applicant's arguments have been fully considered but they are not persuasive. One of skill in the art would have known that lung cancer (like most cancers) develops as a multistage process. For example, see the 1st sentence, of the 1st full paragraph, in the right column of Herzog et al. (Journal of Cellular Biochemistry Supplements, 1997, Vol. 28/29, pp. 49-63; provided for evidentiary purposes). As discussed above, the strong anti-tumor promoting activity of the instantly claimed compound, as taught by Tanaka et al., would have motivated the skilled artisan to test the effectiveness of the

compound in inhibiting tumorigenesis in other tissues, including the lung (a very prevalent form of cancer). The teaching by Fan et al. of a correlation between the mouse skin tumor and lung adenoma assays was cited for providing *further* motivation for one of ordinary skill to test the compound for effectiveness in inhibiting lung tumorigenesis. Fan et al. provide a correlation of carcinogenic activity between the mouse skin tumor assay and the mouse lung adenoma assay (e.g., similar lowest systemic dose having a positive carcinogenic response in both assays).

Conclusion

11. Claims 1-6 are rejected.

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GREGG POLANSKY whose telephone number is (571)272-9070. The examiner can normally be reached on Mon-Thur 9:30 A.M. - 7:00 P.M. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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